PATENT
Docket No. 240042052403

CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this correspondence is being facsimile transmitted to the United States Patent and Trademark Office on February 5, 2002.

Rhea Amid

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Jeffrey S. Glenn

Serial No.: 09/687,267

Filing Date: October 13, 2000

For: METHOD FOR INHIBITION OF VIRAL MORPHOGENESIS

Examiner: B. Brumback

Group Art Unit: 1642

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4-502

DECLARATION OF JEFFREY S. GLENN PURSUANT TO 37 C.F.R. §1.132

BOX AF
Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, Jeffrey S. Glenn, declare as follows:

1. I am the sole inventor of the subject matter claimed in the above-referenced application.

2. I have conducted experiments demonstrating that:

1) the prenylation inhibitors FTI-277 and FTI-2153 can be used to treat hepatitis delta virus (HDV) infection *in vivo*; and

2) FTI-277 and FTI-2153 can effectively inhibit the production of HDV virions at a concentration that is not toxic to the testing animals.

EXHIBIT A
SN 09/687,267

These experimental results are set forth in the following paragraphs 3-4 and in attached Figures 1A-D.

3. HBV-transgenic mice were inoculated by hydrodynamic transfection to initiate authentic HDV genome replication. Mice were treated for one week by IP injection with vehicle alone (Figure 1A and 1B, lanes 1 and 6), vehicle + 50 mg/kg/day FTI-277 (Figure 1A and 1B, lanes 2-5), or vehicle + 50 mg/kg/day FTI-2153 (Figure 1A and 1B, lanes 7-10). Serum samples were then analyzed for HDV virions by RT-PCR analysis (Figure 1A and 1B, lanes 1-10). The primers used in the RT-PCR assay yield a 540 bp fragment only in the presence of circular viral genomic RNA, as found in virions. The production and release of HDV virions into the serum was completely eliminated in the groups treated with prenylation inhibitors.

4. Non-specific toxicity of the FTI-277 and FTI-2153 on the testing animals was assessed by alanine aminotransferase (ALT) assays, which is a standard "liver function" test, (Figure 1C and 1D) performed on aliquots of the corresponding serum samples from Figure 1A and 1B. For the dosages tested, on average, animals treated with FTI-277 have the same level of ALT as the placebo and animals treated with FTI-2153 have lower level of ALT than the placebo.

5. Taken together, the above results demonstrate that the prenylation inhibitors FTI-277 and FTI-2153 can effectively inhibit HDV virion production *in vivo*. This inhibition is not associated with, and cannot be explained by, non-specific toxicity in the testing animals.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are

punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

Executed at Palo Alto, California, on February 5, 2002.

Jeffrey S. Glenn